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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/502,359	11/30/2004	Luis Enjuanes Sanchez	033644-003	8116

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EXAMINER
HUMPHREY, LOUISE WANG ZHIYING

ART UNIT	PAPER NUMBER
1648	

NOTIFICATION DATE	DELIVERY MODE
10/01/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/502,359	SANCHEZ ET AL.	
	Examiner	Art Unit	
	Louise Humphrey, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *7-18 and 21-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,19 and 20* is/are rejected.

7)☒ Claim(s) *4* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 July 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/30/04,3/21/05,7/9/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Office acknowledges the receipt of Applicant's election and Amendment, filed on 09 July 2007. Claims 1-23 are pending.

Election/Restriction

Applicant elects Group I, claims 1-6, 19 and 20, with traverse. The traversal is on the grounds that the cited publication by Motokawa *et al.* fails to disclose or make obvious the limitation of the encapsidation sequence of a group 1 coronavirus.

Applicant's traversal is not persuasive because the shared same technical feature among Group I-IV is not closely limited to the encapsidation sequence of a group 1 coronavirus. The corresponding technical feature of Group I-IV is a complete or partial genome of a group 1 coronavirus, which is not a contribution over the prior art disclosed by Motokawa et al. (1996) as set forth in the Restriction Requirement mailed on 07 February 2007. PCT Rule 13.1 states: "The international application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept." Accordingly, where there is more than one inventive concept, as is the case here as outlined in the previous Office Action on page 2, the requirement of unity of invention is not met, and thus, the claimed invention cannot be said to have unity of invention.

The restriction among the different products that may be used in the claimed methods is maintained.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-23 are pending. Claims 7-18 and 21-23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention/species/sequence. Claims 1-6, 19 and 20 are examined.

Information Disclosure Statement

The initialed and dated copies of Applicant's IDS form 1449, filed on 30 November 2004, 21 March 2005, and 09 July 2007, respectively, are attached to the instant Office action.

Claim Objections

Claims 4 is objected to because claim 4 has an open limitation "comprising" while its base claim has a closed limitation "consisting" in the claim language.

Appropriate correction is required.

Claim Rejections - 35 USC § 112, 2nd ¶

The following is a quotation of the second paragraph of 35 U.S.C. §112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6, 19 and 20 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites "a nucleic acid sequence complementary to either said sequence in a) or said sequence in b)" in part c) and renders the claim indefinite. It is unclear

whether the limitation is a sequence complementary to the full length or the partial fragment of said sequences. For examination purposes, the complementary sequence is considered a "full-length complementary" sequence.

Claim 1 also recites nucleotide positions in the absence of a reference viral isolate or strain name. Due to the evolution of group 1 coronaviruses through error-prone replication, there is a multitude of strains or isolates of each type of group 1 coronavirus with substantially different nucleotide and amino acid sequences. The skilled artisan would not know whether the nucleotide at one position number in one strain is referring to the same nucleotide at the same position in another strain. Even within the same strain, the nucleotide in a genome sequence would be different from the nucleotide at the same position number in a cDNA sequence. It is unclear whether the position number refers to a nucleotide in the coding sequence or in introns within the viral genome. Therefore, position numbers in the absence of a reference strain or isolate name is vague and indefinite.

Claims 2-6, 19 and 20 are rejected for depending from claim 1.

Clarification and/or correction are required.

Claim Rejections - 35 USC § 112, 1st ¶, Written Description

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 5, 6, 19 and 20 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The factors considered in the Written Description requirement are (1) *level of skill and knowledge in the art*, (2) *partial structure*, (3) *physical and/or chemical properties*, (4) *functional characteristics alone or coupled with a known or disclosed correlation between structure and function*, and the (5) *method of making the claimed invention*. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." M.P.E.P. §2163.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, at the time the invention was made, of the specific subject matter claimed. A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or of a recitation of structural features common to the members of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 199 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In *Regents of the University of California v. Eli Lilly & Co.*, the court indicated that, while applicants are not required to disclose every species

encompassed by a genus, the description of the genus is achieved by the recitation of a representative number of species falling within the scope of the claimed genus. Although the M.P.E.P. does not define what constitutes a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad genus. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

In the instant case, the claims are directed to any of the following four nucleic acid sequences:

(a) a nucleic acid sequence including the encapsidation sequence (ES) and consisting of nucleotide 100 to 649, or the nucleotide 100 to 649 of the genome of a group 1 coronavirus;

(b) a nucleic acid sequence analogous to said sequence in (a);

(c) the full-length complement of said sequence in (a) or (b); or

(d) a nucleic acid sequence with a secondary structure similar to that of an encapsidation sequence (ES) of a group 1 coronavirus, independent of the primary nucleotide sequence.

The claims are drawn to a genus of group 1 coronavirus ES sequences. The limitations "analogous" and "with a secondary structure similar to that of an ES" encompass all structural homologs, synthetic analogs and functional equivalents. The claims encompass an inordinate number of species that are neither described nor contemplated by Applicants.

Applicants have not conveyed possession of the entire genus of the invention with reasonable clarity to one skilled in the art. While the specification broadly states nucleotide 100 to nucleotide 649 of the genome of a group 1 coronavirus (page 5, 1st ¶), Applicants admit on page 2 in the summary that only the region of the TGEV virus genome that includes ES has been localized. The specification only provides a clear description for nucleotide 100 to nucleotide 649 of the cDNA of the porcine transmissible gastroenteritis virus (TGEV) PUR-46 MAD isolate (page 6, 1st ¶), which is SEQ ID NO:1. SEQ ID NO:1 alone does not constitute a representative number of species to adequately describe such a broad genus of group 1 coronavirus ES-containing sequences. Furthermore, there is no identification of any common sequence structure that correlates with the ES of all group 1 coronaviruses. The nucleotide 100 to 649 of the genome of a group 1 coronavirus is not a specific common sequence shared by all strains of all species of group 1 coronaviruses. There is no evidence showing that SEQ ID NO:1 is a common sequence shared by the genomes of all strains of group 1 coronavirus at position 100 to 649. The specification pressumes that the nucleotides at the same position are the same in both cDNA and genome sequences. Without any supporting evidence, the specification also speculates that the ES-containing sequence of every other strain of TGEV as well as other group 1 coronavirus is in the same position as the ES sequence in the cDNA sequence of the PUR-46 MAD strain of TGEV. The specification further leaps to speculate on sequences that are analogous or functionally equivalent to the group 1 coronavirus ES-containing sequence. However, the state of art at the time of invention shows evolution-driven genetic diversity of TGEV

strains (Penzes *et al.*, Virus Genes 23:1, p. 105-118, 2001) and genetic variations that result in a different location of the packaging signal in TGEV genome when compared to the genomes of other group 1 coronaviruses such as the bovine coronavirus and mouse hepatitis coronavirus (Escors et al., Journal of Virology, 77;14, p.7890-7902, 2003). Thus, the claimed invention lacks an adequate written description. As a result, one of skill in the art could not conclude that Applicant was in possession of the claimed methods at the time of the invention. Therefore, claims 1-3, 5, 6, 19 and 20 do not meet the written description provision of 35 U.S.C. §112, first paragraph.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (page 1115).

Claim Rejections - 35 USC § 112, 1st ¶, enablement

Claims 1-3, 5, 6, 19 and 20 are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for a nucleic acid consisting of from nucleotide 100 to nucleotide 649 of the cDNA of the PUR-46 MAD strain of TGEV, does not reasonably provide enablement for a nucleic acid consisting of from nucleotide 100 to nucleotide 649 of the genome of a group 1 coronavirus. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors (MPEP §2164.01(a)). See, *In re Wands*, 8 USPQ2d 1400, at 1404 (CAFC 1988); and

Ex Parte Forman, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *Id.* While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered.

The instant claims are directed to any of the following four nucleic acid sequences:

(a) a nucleic acid sequence including the encapsidation sequence (ES) and consisting of nucleotide 100 to 649, or the nucleotide 100 to 649 of the genome of a group 1 coronavirus;

(b) a nucleic acid sequence analogous to said sequence in (a);

(c) the full-length complement of said sequence in (a) or (b); or

(d) a nucleic acid sequence with a secondary structure similar to that of an encapsidation sequence (ES) of a group 1 coronavirus, independent of the primary nucleotide sequence.

The disclosure fails to provide adequate support for the full scope of the invention for reasons as follows:

While the specification broadly states nucleotide 100 to nucleotide 649 of the genome of a group 1 coronavirus (page 5, 1st ¶), Applicants admit in the summary of invention that only the ES region of the TGEV virus genome has been localized (page

2). The specification only provides a clear description for nucleotide 100 to nucleotide 649 of the cDNA of the porcine transmissible gastroenteritis virus (TGEV) PUR-46 MAD isolate (page 6, 1st ¶), which is SEQ ID NO:1.

SEQ ID NO:1 alone does not constitute a representative number of species to adequately describe such a broad genus of group 1 coronavirus ES-containing sequences. Furthermore, there is no identification of any common sequence structure that correlates with the ES of all group 1 coronaviruses. The nucleotide 100 to 649 of the genome of a group 1 coronavirus is not a specific common sequence shared by all strains of all species of group 1 coronaviruses. Without any supporting evidence, the specification presumes that the nucleotides at the same positions are the same in both cDNA and genome sequences. The specification also speculates that the ES region of every other strain of TGEV as well as other group 1 coronavirus is in the same position as the ES region in the cDNA sequence of the PUR-46 MAD strain of TGEV. The specification further leaps to speculate on sequences that are analogous or functionally equivalent to the group 1 coronavirus ES-containing sequence. However, the state of art at the time of invention shows evolution-driven genetic diversity of TGEV strains (Penzes *et al.*, Virus Genes 23:1, p. 105-118, 2001) and genetic variations that result in a different location of the packaging signal in TGEV genome when compared to the genomes of other group 1 coronaviruses such as the bovine coronavirus and mouse hepatitis coronavirus (Escors et al., Journal of Virology, 77;14, p.7890-7902, 2003). The prior art teaches unpredictable position numbers of the ES region in the genome sequences and fails to provide sufficient illumination pertaining to the structural

guidance of the claimed ES region of any group 1 coronavirus and its analogs or functional equivalents.

Amount of experimentation necessary. Applicants have extended an invitation to identify all ES sequences in every other strain of group 1 coronaviruses, all analogs and functional variants. In regards to the "nucleotide 100 to nucleotide 649 of the genome of a group 1 coronavirus", this is pure speculation on Applicant's part that the nucleotide position numbers set forth in the claims can define the ES region in the genome of any strain of any group 1 coronavirus. There is little specific guidance in the art or specification. While Applicant is not required to set forth working examples, the specification must set forth sufficient teachings to allow one to make the claimed invention. The only working example is SEQ ID NO:1, which is not commensurate in scope with the claimed invention. There is no evidence showing that SEQ ID NO:1 is a common sequence shared by the genomes of all strains of group 1 coronavirus at position 100 to 649. Thus, the instant invention, based on the evidence as a whole, in light of the factors articulated by the court in *In re Wands*, lacks an enabling disclosure.

For the reasons discussed above, it would require undue and unpredictable experimentation for one skilled in the art to use the claimed methods.

Remarks

No claim is allowable.

Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP §714.02 and §2163.06.

Correspondence

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey, Ph.D. whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9:30 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Jeffrey Parkin, Ph.D.
Primary Examiner
10 September 2007

Louise Humphrey, Ph.D.
Assistant Examiner